REMARKS

Claims 2-5 and 8-16 are currently pending in the application. Claims 3-5 and 8-14 are withdrawn from consideration. Claim 15 is in independent form.

Claims 2, 15, and 16 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement because of limitations that are new concepts because they do not have literal support in the as-filed specification by way of generic disclosure, nor are there specific examples. Specifically, the Office Action holds that the limitation "the products consisting essentially of the secretions from the stem cells" has no support in the as-filed specification as the generic disclosure relates to the potential benefits of the stem cells in combinations with their secretions but not to the secretions alone as a sole therapeutic agent.

With respect to the limitation "the products consisting essentially of the secretions from the stem cells," the Office Action refers to the paragraph at lines 23-31 on page 4 of the specification wherein it is stated that "the purpose of the present invention is to utilize stem cells, supernatant from stem cells, the secretions resulting from the interaction of stem cells and other cells (e.g., stem cell products), *or* compounds that increase the amount of secretions present at a site, for treating heart failure" (emphasis added). Applicants point out the use of alternative language in this paragraph, italicized above, meaning that *any one* of stem cell, supernatant, secretions, or compounds increasing secretions can be administered. There is no requirement that any of these components be used together.

Applicants point out that the specification states that "the stem cells *or products thereof* can be administered at the specific location of the injury." Specification, page 9, lines 11-12, emphasis added. There is no requirement that the stem cells and the

stem cell products must be administered together, as they can be administered separately or together based on lines 11-12 of page 9. The statement of the Office Action referring to page 9, lines 15-18 of the specification that the stem cells can produce products at the site of administration is referring to the case when stem cells and stem cell products are administered together. Thus, stem cells alone can be administered that will produce secretions *in vivo*; however, as the paragraph also states, these secretions can be administered by themselves without the stem cells. Therefore, the specification is fully supported for the limitation of "the products consisting essentially of the secretions from the stem cells."

The Office Action further holds that the limitation "separating the stem cells from a supernatant, the supernatant containing the products consisting essentially of secretions from the stem cells; and administering the products consisting essentially of the secretions from the stem cells" has no support in the as-filed specification. With respect to Applicants' previous argument that one of skill in the art would have known how to obtain and to separate a supernatant from the stem cells, the Office Action holds that the rejection is a matter of written description, not a question of what one of skill in the art would or would not have known.

With respect to this limitation, Applicants respectfully point out that there is no requirement to include in the specification what is already known in the art.

"[A] patent need not teach, and preferably omits, what is well known in the art." *Hybritech Inc v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986).

One utilizing the teachings of this application would be able to perform a separation of the supernatant, as separating cells and cell products from supernatant

is a basic skill that one skilled in the art would be able to perform. Such separation processes include, for example, centrifugation. There is no reason why Applicants should be required to explain how to perform a simple laboratory technique, when, as stated above, the courts have concluded that such information is preferably left out of the application. Therefore, the limitation of "separating the stem cells from a supernatant" is fully supported by the specification. Reconsideration of the rejection under 35 U.S.C. §112 to claims 2, 15, and 16 is respectfully requested.

Claims 2, 15, and 16 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Pierpaolli, et al. Specifically, the Office Action holds that Pierpaolli, et al. discloses a method comprising the steps of a) isolating stem cells from harvested marrow, b) growing the stem cells without differentiation in medium or storing cells in the medium, c) enriching the medium containing the stem cells under hypoxia or storing cells in a closed vessel in a refrigerator, d) separating the stem cells from a supernatant, the supernatant containing "products consisting essentially of secretions from the stem cell" that would be "MRF", and e) administering the MRF intravenously. Reconsideration of the rejection under 35 U.S.C. § 102(b), as anticipated by Pierpaolli, et al., as applied to the claims is respectfully requested. Anticipation has always been held to require absolute identity in structure between the claimed structure and a structure disclosed in a single reference.

Pierpaolli, et al. teaches the administration of marrow regulating factors (MRF) obtained by suspending bone marrow in supernatant and then centrifuging the supernatant, passing the supernatant over a filter, and collecting the material that did not pass through the filter to administer to mice (p. 219-221). This reference is concerned with immune system reconstitution, and does not teach anything about improving cardiac function.

First, with respect to the rejection under §112 above, Applicants point out that from this reference, it is clear that separating a material from a supernatant is known in the art. Second, with respect to the present §102 rejection, Pierpaolli does not disclose critical steps of independent claim 15. There is no disclosure whatsoever of growing stem cells without differentiation in medium, enriching the medium containing the stem cells, separating the stem cells from the supernatant wherein the supernatant contains products consisting essentially of secretions from the stem cells, and administering the products consisting essentially of the secretions from the stem cells. Pierpaolli, et al. does not use the medium of the present invention, which is specially prepared and contains "agents that allowed for not only mesenchymal stem cell growth without differentiation, but also for the direct adherence of only the mesenchymal stem cells to the plastic or glass surface area of the culture dish. By producing a medium that allowed for the selective attachment of the desired mesenchymal stem sells that were present in the marrow samples in very minute amounts, it was possible to separate the mesenchymal stem cells from other cells ... present in the bone marrow." Specification, page 10, lines 10-18. Because Pierpaolli, et al. is not using such a medium, the same products of the bone marrow will not be collected. Pierpaolli, et al. does not enrich its supernatant. Further, Pierpaolli, et al. does not teach administering the supernatant itself, but rather the filtered product separated from the supernatant. The supernatant is not used at all. According to the presently pending independent claim, Applicants separate out the stem cells, and administer the supernatant which contains the secreted stem cell products. Also, Pierpaolli, et al. is not administering only secretions of stem cells, but rather an ultrafiltration fraction of MW > 100,000 MRF.

Therefore, since the Pierpaolli, et al. reference does not disclose growing stem cells without differentiation in medium, enriching the medium containing the stem cells, separating the stem cells from the supernatant wherein the supernatant

contains products consisting essentially of secretions from the stem cells, and administering the products consisting essentially of the secretions from the stem cells as set forth in the presently pending independent claim, the claim is patentable over the Pierpaolli, et al. reference and reconsideration of the rejection is respectfully requested.

Claims 2, 15, and 16 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 7,097,832 to Kornowski, et al (hereinafter the '832 patent). Specifically, the Office Action holds that the '832 patent discloses and/or suggests a method of improving cardiac function wherein the method comprises steps of culturing bone marrow stem cells under hypoxia conditions for enrichment in the secretions from the stem cells and administering bone marrow stem cells and the bone marrow secretion products. The '832 patent discloses that the bone marrow secreted factors are necessary to promote new blood vessel growth and to restore function of ischemic heart and it also suggests administration of the bone marrow cell secretions. Therefore, the Office Action holds that it would have been obvious to administer the bone marrow stem cell secretions to the ischemic heart with a reasonable expectation of success. Reconsideration of the rejection under 35 U.S.C. §103(a), as being unpatentable over the '832 patent is respectfully requested.

The '832 patent discloses a method of treating cardiac or myocardial conditions by administering autologous bone marrow. The marrow can be exposed to hypoxia to activate the transcription factor HIF-1. The marrow is injected into a patient and there it secretes angiogenic factors. There is no disclosure or suggestion of performing the method disclosed by Applicants in presently pending independent claim 15. It is already known in the art, as Applicants explain in the background section of the specification, that marrow itself can be injected into the myocardium and stromal cells in the marrow can show growth potential. No one, however, has

shown or suggested that secretions from stem cells can be separated and administered alone without administering the actual stem cells as well, i.e. only administering the supernatant separated from the stem cells, which themselves have been specifically separated from the bone marrow. There cannot be a reasonable expectation of success from the disclosure of the '832 patent based on administering bone marrow in its entirety when no experiments have been performed administering only the secretions of stem cells.

Since neither the '832 patent alone or in combination with knowledge in the art suggests the currently claimed invention, it is consequently respectfully submitted that the claims are clearly patentable over the combination, even if the combination were to be applied in opposition to applicable law, and reconsideration of the rejection is respectfully requested.

The remaining dependent claims not specifically discussed herein are ultimately dependent upon the independent claims. References as applied against these dependent claims do not make up for the deficiencies of those references as discussed above, and the prior art references do not disclose the characterizing features of the independent claims discussed above. Hence, it is respectfully submitted that all of the pending claims are patentable over the prior art.

In view of the present amendment and foregoing remarks, reconsideration of the rejections and advancement of the case to issue are respectfully requested.

The Commissioner is authorized to charge any fee or credit any overpayment in connection with this communication to our Deposit Account No. 11-1449.

Respectfully submitted,

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Connie Herty